DNA confinement in nanochannels: physics and biological applications

DNA is the central storage molecule of genetic information in the cell, and reading that information is a central problem in biology. While sequencing technology has made enormous advances over the past decade, there is growing interest in platforms that can readout genetic information directly from long single DNA molecules, with the ultimate goal of single-cell, single-genome analysis. Such a capability would obviate the need for ensemble averaging over heterogeneous cellular populations and eliminate uncertainties introduced by cloning and molecular amplification steps (thus enabling direct assessment of the genome in its native state). In this review, we will discuss how the information contained in genomic-length single DNA molecules can be accessed via physical confinement in nanochannels. Due to self-avoidance interactions, DNA molecules will stretch out when confined in nanochannels, creating a linear unscrolling of the genome along the channel for analysis. We will first review the fundamental physics of DNA nanochannel confinement—including the effect of varying ionic strength—and then discuss recent applications of these systems to genomic mapping. Apart from the intense biological interest in extracting linear sequence information from elongated DNA molecules, from a physics view these systems are fascinating as they enable probing of single-molecule conformation in environments with dimensions that intersect key physical length-scales in the 1 nm to 100μm range. (Some figures may appear in colour only in the online journal)